WEST Search History

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DATE: Monday, August 16, 2004

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=AND	
☐	L1	neospor$	491
☐	L2	L1 same temperat$	21
☐	L3	L1 near25 (mutant$ or mutation$ or mutagenesis or attenuat$ or avirulent or a-virulent or nonpathogenic or non-pathogenic or modified or modification or inactivation or inactivated)	35

END OF SEARCH HISTORY

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Search Results - Record(s) 1 through 35 of 35 returned.

1. 20040131633. 30 Jun 03. 08 Jul 04. Parasite antigens. Ellis, John Timothy, et al. 424/190.1; 530/350 A61K039/02 C07K014/195.

2. 20040062772. 24 Sep 03. 01 Apr 04. Attenuated live neospora vaccine. Brake, David A., et al. 424/184.1; 424/274.1 435/254.2 A61K039/00 A61K039/38 C12N001/18.

3. 20040006319. 20 Jun 03. 08 Jan 04. Wound therapy device. Lina, Cesar Z., et al. 604/304; A61F013/00.

4. 20030185852. 04 Apr 03. 02 Oct 03. Parasitic protozoan isolate. Ellis, John Timothy, et al. 424/191.1; 424/269.1 435/258.1 A61K039/005 A61K039/008 C12N001/10.

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7. 20020165373. 21 Sep 01. 07 Nov 02. Recombinant neospora antigens and their uses. Conrad, Patricia C., et al. 536/23.1; C07H021/02 C07H021/04.

8. 20020146436. 02 Apr 02. 10 Oct 02. Neospora vaccines. Choromanski, Leszek J., et al. 424/269.1; 435/258.1 A61K039/002 C12N001/10.

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10. 20020044952. 12 Sep 01. 18 Apr 02. Attenuated live neospora vaccine. Brake, David A., et al. 424/265.1; 435/243 A61K039/002 C12N001/00.

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12. 6716423. 10 Jul 00; 06 Apr 04. Recombinant neospora antigens and their uses. Conrad; Patricia A., et al. 424/93.1; 424/184.1 424/234.1 424/93.7. A61K039/00 A61K039/38 A61K039/02 A01N063/00 A01N065/00.

13. 6695823. 07 Apr 00; 24 Feb 04. Wound therapy device. Lina; Cesar Z., et al. 604/304; 602/43. A61F013/00.

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15. 6600027. 25 Mar 99; 29 Jul 03. Polynucleotide molecules encoding neospora proteins. Krishnan; B. Rajendra, et al. 536/23.1; 435/252.3 435/320.1 435/69.1 536/23.4 536/23.5 536/24.32.

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Terms	Documents
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☐ 1. 20040131633. 30 Jun 03. 08 Jul 04. Parasite antigens. Ellis, John Timothy, et al. 424/190.1; 530/350 A61K039/02 C07K014/195.

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☐ 9. 20020058046. 09 Nov 01. 16 May 02. Neospora vaccine. Brake, David A., et al. 424/265.1; A61K039/002.

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☐ 11. 6716423. 10 Jul 00; 06 Apr 04. Recombinant neospora antigens and their uses. Conrad; Patricia A., et al. 424/93.1; 424/184.1 424/234.1 424/93.7. A61K039/00 A61K039/38 A61K039/02 A01N063/00 A01N065/00.

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L3: Entry 1 of 35 File: PGPB Jul 8, 2004

PGPUB-DOCUMENT-NUMBER: 20040131633
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040131633 A1

TITLE: Parasite antigens

PUBLICATION-DATE: July 8, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ellis, John Timothy	Hornsby New South Wales		AU	
Atkinson, Robert	Irvinebank		AU	
Ryce, Cheryl	New South Wales		AU	
Quinn, Helen Elizabeth	Chapel Hill		AU	
Miller, Catherine Margaret	Roseville		AU	
Morrison, David Andrew	Uppsala		SE	

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	COUNTRY	TYPE CODE
University of Technology, Sydney				03

APPL-NO: 10/ 608436 [PALM]
DATE FILED: June 30, 2003

RELATED-US-APPL-DATA:
Application 10/608436 is a continuation-in-part-of US application 09/959246, filed January 10, 2002, PENDING
Application 09/959246 is a a-371-of-international WO application PC/T/AU00/00354, filed April 20, 2000, UNKNOWN

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
AU	PP 9928	1999AU-PP 9928	April 21, 1999
WO	PCT/AU00/00354	2000WO-PCT/AU00/00354	April 20, 2000
WO	PCT/AU99/00405	1999WO-PCT/AU99/00405	May 26, 1999

INT-CL: [07] A61 K 39/02, C07 K 14/195

US-CL-PUBLISHED: 424/190.1; 530/350
US-CL-CURRENT: 424/190.1; 530/350

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

The present invention relates to polypeptides from N. caninum which are capable of raising an immune response when administered to an animal. Such polypeptides can be used in vaccination strategies for protecting animals, such as cows and dogs, from neosporosis.

First Hit

L2: Entry 2 of 21 File: PGPB Apr 29, 2004

DOCUMENT-IDENTIFIER: US 20040081666 A1
TITLE: Cattle reproductive disease vaccines

Summary of Invention Paragraph:
[0022] The term "combination vaccine" is meant a bivalent or multivalent combination of antigens including modified live antigens and/or inactivated antigens. In accordance with the present invention a combination vaccine can comprise modified live infectious IBR, PI3, BRSV and inactivated BVDV Types 1 and 2, one or more antigens such as but not limited to Leptospira canicola, Leptospira grippotyphosa, Leptospira borgpetersenii hardio-prajitno, Leptospira icterohaemmorrhagia, Leptospira interrogans pomona, Leptospira borgpetersenii hardjo-bovis, Leptospira bratislava, Campylobacter fetus, Neospora caninum, Trichomonus fetus, Mycoplasma bovis, Haemophilus somnus, Mannheimia haemolytica and Pasturella multocida, a veterinary acceptable carrier and an adjuvant. In a preferred embodiment the modified live IBR component is temperature sensitive IBR. In another preferred embodiment the BVDV Type 2 component is cytopathic (cpBVD-2 strain 53637-ATCC No. PTA-4859) and the BVDV Type 1 component is cytopathic 5960 (cpBDV-1 strain 5960-National Animal Disease Center, United States Department of Agriculture, Ames, Iowa). The present invention also contemplates non-cytopathic BVDV Type 1 and Type 2 strains. In still another preferred embodiment, the modified live antigens are desiccated, lyophilized or vitrified.

First Hit

L2: Entry 3 of 21 File: PGPB Apr 1, 2004

PGPUB-DOCUMENT-NUMBER: 20040062772
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040062772 A1

TITLE: Attenuated live neospora vaccine

PUBLICATION-DATE: April 1, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Brake, David A.	East Lyme	CT	US	
Blagburn, Byron L.	Auburn	AL	US	
Lindsay, David S.	Christiansburg	VA	US	

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	COUNTRY	TYPE CODE
PFIZER INC	NEW YORK	NY		02

APPL-NO: 10/ 669941 [PALM]
DATE FILED: September 24, 2003

RELATED-US-APPL-DATA:
Application 10/669941 is a continuation-of US application 09/952388, filed September 12, 2001, US Patent No. 6656479
Application 09/952388 is a continuation-of US application 09/260414, filed February 26, 1999, ABANDONED
Application 09/260414 is a continuation-of US application 08/967744, filed November 10, 1997, ABANDONED
Application is a non-provisional-of-provisional application 60/031248, filed November 12, 1996,

INT-CL: [07] A61 K 39/00, A61 K 39/38, C12 N 1/18

US-CL-PUBLISHED: 424/184.1; 424/274.1, 435/254.2
US-CL-CURRENT: 424/184.1; 424/274.1, 435/254.2

ABSTRACT:

The present invention provides attenuated live cultures of the pathogenic protozoan parasite, Neospora, and live vaccines against neosporosis prepared therefrom which are useful in the prevention of clinical disease and abortion in mammals.

First Hit

L2: Entry 7 of 21 File: PGPB Oct 10, 2002

PGPUB-DOCUMENT-NUMBER: 20020146436
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020146436 A1

TITLE: Neospora vaccines

PUBLICATION-DATE: October 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Choromanski, Leszek J.	Lenexa	KS	US	
Brown, Karen K.	Parkville	MD	US	

APPL-NO: 10/ 115478 [PALM]
DATE FILED: April 2, 2002

RELATED-US-APPL-DATA:
Application 10/115478 is a division-of US application 08/954531, filed October 20, 1997, PENDING

INT-CL: [07] A61 K 39/002, C12 N 1/10

US-CL-PUBLISHED: 424/269.1; 435/258.1
US-CL-CURRENT: 424/269.1; 435/258.1

ABSTRACT:

A Neospora caninum vaccine comprising tissue culture grown Neospora and methods of making and using said vaccines. Neospora caninum vaccines described include those containing whole Neospora tachyzoites, extracts of Neospora tachyzoites and protective antigen subunits of Neospora tachyzoites. The vaccines of this invention may be inactivated or modified live and contain adjuvants and/or stabilizers. The vaccines of this invention may be in a liquid or lyophilized form.

First Hit

L2: Entry 9 of 21 File: PGPB May 16, 2002

PGPUB-DOCUMENT-NUMBER: 20020058046
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020058046 A1

TITLE: Neospora vaccine

PUBLICATION-DATE: May 16, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Brake, David A.	East Lyme	CT	US	
Campos, Manuel	Stonington	CT	US	

US-CL-CURRENT: 424/265.1

CLAIMS:

We claim:

1. An homogenate prepared from cells of Neospora which is capable of inducing a protective response against neosporosis in a mammal.

2. The homogenate of claim 1, wherein the species of Neospora from which the homogenate is prepared is N. caninum.

3. The homogenate of claim 1, which is capable of inducing the production of antibodies that recognize one or more antigenic components present in an homogenate of cells of N. caninum strain NC-1.

4. The homogenate of claim 3, wherein the species of Neospora from which the homogenate is prepared is N. caninum.

5. The homogenate of claim 4, wherein the strain of N. caninum from which the homogenate is prepared is NC-1.

6. The homogenate of claim 1 which is prepared from tachyzoites.

7. A vaccine to protect a mammal against neosporosis, comprising an immunologically effective amount of an homogenate prepared from cells of Neospora, which homogenate is capable of inducing a protective response against neosporosis in a mammal, and a veterinarily acceptable carrier.

8. The vaccine of claim 7, wherein the species of Neospora from which the homogenate is prepared is N. caninum.

9. The vaccine of claim 7, which is capable of inducing the production of antibodies that recognize one or more antigenic components present in an homogenate of cells of N. caninum strain NC-1.

10. The vaccine of claim 9, wherein the species of Neospora from which the homogenate of the vaccine is prepared is N. caninum.

11. The vaccine of claim 10, wherein the strain of N. caninum from which the homogenate of the vaccine is prepared is NC-1.

12. The vaccine of claim 7. wherein the homogenate is prepared from tachyzoites.

13. The vaccine of claim 7, further comprising one or more additional immunomodulatory components

14. The vaccine of claim 13, in which the additional immunomodulatory component is an adjuvant.

15. The vaccine of claim 14, in which the adjuvant is selected from the group consisting of the RIBI adjuvant system (Ribi Inc.), alum, aluminum hydroxide gel. an an oil-in-water emulsion, a water-in-oil emulsion, Block co polymer, QS-21, SAF-M, AMPHIGEN.RTM. adjuvant, saponin, Quil A, monophosphoryl lipid A, and Avridine lipid-lipid-amine adjuvant.

16. The vaccine of claim 15, in which the adjuvant is an oil-in-water emulsion selected from the group consisting of SEAM62 and SEAM 1/2.

17. The vaccine of claim 13, in which the additional immunomodulatory component is a a cytokine.

18. The vaccine of claim 7, wherein the Neospora cells from which the homogenate is prepared have been modified to delete the expression of one or more antigenic components normally associated with Neospora cells or a homogenate prepared therefrom.

19. A method for preparing a vaccine that protects a mammal against neosporosis, comprising homogenizing cells from Neospora to produce an homogenate capable of inducing a protective response against neosporosis in a mammal, and combining an immunologically effective amount of the homogenate with a veterinarily acceptable carrier.

20. The method of claim 19, wherein the species of Neospora from which the homogenate is prepared is N. caninum.

21. The method of claim 19, wherein the vaccine is capable of inducing the production of antibodies that recognize one or more antigenic components present in an homogenate of cells of N. caninum strain NC-1.

22. The method of claim 21, wherein the species of Neospora from which the homogenate of the vaccine is prepared is N. caninum.

23. The method of claim 22, wherein the strain of N. caninum from which the homogenate of the vaccine is prepared is NC-1.

24. The method of claim 19, wherein the cells that are homogenized are tachyzoites.

25. The method of claim 24, wherein the tachyzoites are homogenized by freeze/thawing and sonication.

26. The method of claim 19, further comprising adding one or more additional

immunomodulatory components to the vaccine.

27. The method of claim 26. wherein the additional immunomodulatory component is an adjuvant.

28. The method of claim 26, wherein the additional immunomodulatory component is a cytokine.

29. A method for protecting a mammal against neosporosis, comprising administering to the mammal a vaccine comprising an immunologically effective amount of an homogenate prepared from cells of Neospora, which homogenate is capable of inducing a protective response against neosporosis in a mammal, and a veterinarily acceptable acceptable carrier.

30. The method of claim 29, wherein the species of Neospora from which the homogenate is prepared is N. caninum.

31. The method of claim 29, wherein the vaccine is capable of inducing the production of antibodies that recognize one or more antigenic components present in an homogenate of cells of N. caninum strain NC-1.

32. The method of claim 31, wherein the species of Neospora from which the homogenate of the vaccine is prepared is N. caninum.

33. The method of claim 32, wherein the strain of N. caninum from which the homogenate of the vaccine is prepared is NC-1.

34. The method of claim 29, wherein the homogenate of the vaccine is prepared from tachyzoites.

35. The method of claim 29, wherein the vaccine further comprises one or more additional immunomodulatory components

36. The method of claim 35, wherein the additional immunomodulatory component is an adjuvant.

37. The method of claim 35, wherein the additional immunomodulatory component is a cytokine.

38. The method of claim 29, wherein the vaccine is administered to a mammal of a species selected from the group consisting of dogs, cows, goats, sheep and horses.

39. A combination vaccine for protecting a mammal against neosporosis and, optionally, one or more other diseases or pathological conditions that can afflict the mammal, which combination vaccine comprises an immunologically effective amount of a first composition comprising an homogenate prepared from cells of Neospora, which homogenate is capable of inducing a protective response against neosporosis in in a mammal; an immunologically effective amount of a second composition capable of inducing a protective response against a disease or pathological condition that can afflict the mammal; and a veterinarily acceptable carrier.

40. The combination vaccine of claim 39, wherein the species of Neospora from which the homogenate of the first composition is prepared is N. caninum.

41. The combination vaccine of claim 39, which is capable of inducing the production production of antibodies that recognize one or more antigenic components present in

an homogenate of cells of N. caninum strain NC-1.

42. The combination vaccine of claim 41, wherein the species of Neospora from which the homogenate of the first composition is prepared is N. caninum.

43. The combination vaccine of claim 42, wherein the strain of N. caninum from which which the homogenate of the first composition is prepared is NC-1.

44. The combination vaccine of claim 39, wherein the homogenate of the first composition is prepared from tachyzoites.

45. The combination vaccine of claim 39, wherein the second composition is capable of inducing in the mammal a protective response against a pathogen selected from the the group consisting of bovine herpes virus, bovine respiratory syncitial virus, bovine viral diarrhea virus, parainfluenza virus types I, II, or III, Leptospira spp., Campylobacter spp., Staphylococcus aureus, Streptococcus agalactiae, Mycoplasma spp., Klebsiella spp., Salmonella spp., rotavirus, coronavirus, rabies, Pasteurella haemolytica, Pasteurelia multocida, Clostridia spp., Tetanus toxoid, E. coli, Cryptosporidium spp., Eimeria spp. and Neospora spp.

46. A kit for vaccinating a mammal against neosporosis, comprising a first container container having an immunologically effective amount of an homogenate prepared from cells of Neospora, which homogenate is capable of inducing a protective response against neosporosis in a mammal, and a second container having a veterinarily acceptable carrier or diluent.

47. An antibody specific to an antigenic component present in an homogenate of Neospora cells.

48. The antibody of claim 47, which is specific to an antigenic component present in in an homogenate prepared from N. caninum cells.

49. The antibody of claim 48, which is specific to an antigenic component present in in an homogenate prepared from cells of N. caninum strain NC-1.

50. The antibody of claim 49, wherein the antigenic component has a molecular weight weight selected from the group consisting of 17-19, 28-30, 33, 37, 46, 48, and 56 kD.

51. The antibody of claim 47, further comprising a detectable label.

First Hit

L2: Entry 10 of 21 File: PGPB Apr 18, 2002

DOCUMENT-IDENTIFIER: US 20020044952 A1
TITLE: Attenuated live neospora vaccine

Summary of Invention Paragraph:
[0021] High serial passage may be carried out by repeated in vitro passaging of cells of a pathogenic strain of Neospora in susceptible host cells until sufficient attenuation occurs. Passaging may be conducted under specific environmental conditions to select for attenuated cells. For example, passaging may be conducted at a temperature below that of the body temperature of the intended mammalian vaccinate to select for temperature-sensitive strains of Neospora that will not grow, or that will only grow at a reduced rate, when administered in a vaccine to the mammal.

Detail Description Paragraph:
[0052] The objective of this study was to establish temperature-sensitive strains of N. caninum (NCTS), and to test the pathogenicity of these strains by analyzing serum antibody response, tissue cyst and brain lesion production, and the development of clinical symptoms in BALB/c mice, which are known to be highly susceptible to neosporosis.

First Hit Fwd Refs

L2: Entry 11 of 21 File: USPT Apr 6, 2004

US-PAT-NO: 6716423
DOCUMENT-IDENTIFIER: US 6716423 B1

TITLE: Recombinant neospora antigens and their uses

DATE-ISSUED: April 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Conrad; Patricia A.	Davis	CA		
Barr; Bradd C.	Davis	CA		
Anderson; Mark L.	Davis	CA		
Sverlow; Karen W.	Vacaville	CA		

US-CL-CURRENT: 424/93.1; 424/184.1, 424/234.1, 424/93.7

CLAIMS:

What is claimed is:

1. A method for obtaining a normal calf from a bovine animal, comprising the steps of: (i) administering to the bovine animal a pharmaceutical composition comprising a pharmaceutically acceptable carrier and an immunogenically effective amount of a bovine Neospora tachyzoite; (ii) breeding the bovine animal; and (iii) obtaining a normal calf from the bovine animal.

2. The method of claim 1, wherein the bovine animal is a cow or heifer.

3. The method of claim 1, wherein the pharmaceutical composition is administered parenterally.

4. The method of claim 1, wherein the isolated bovine Neospora tachyzoite is attenuated.

5. The method of claim 1, wherein the bovine Neospora tachyzoite is selected from the group consisting of ATCC Accession No. 75710 (BPA1) and ATCC Accession Accession No. 75711 (BPA6).

6. A method for protecting a bovine animal from Neospora abortion, the method comprising the administration of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and an immunogenically effective amount of a bovine Neospora antigen, whereby the bovine animal is protected from abortion abortion induced by Neospora infection, wherein the bovine Neospora antigen is an isolated bovine Neospora tachyzoite of ATCC Accession No. 75710 (BPA1) or ATCC Accession No. 75711 (BPA6).

7. The method of claim 6, wherein the bovine animal is a cow or heifer.

First Hit Fwd Refs

L2: Entry 12 of 21 File: USPT Dec 2, 2003

US-PAT-NO: 6656479
DOCUMENT-IDENTIFIER: US 6656479 B2

TITLE: Attenuated live neospora vaccine

DATE-ISSUED: December 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brake; David A	East Lyme	CT		
Blagburn; Byron L	Auburn	AL		
Lindsay; David S	Christiansburg	VA		

US-CL-CURRENT: 424/269.1; 424/258.1, 424/271.1, 424/273.1, 424/93.1, 424/93.2, 435/258.1, 435/69.1

CLAIMS:

We claim:

1. A live culture of cells of an attenuated strain of a species of Neosyora, wherein the strain is NCTS-8 which is present in MARC145 monkey kidney cells having ATCC accession No. CRL12230.

2. A vaccine for protecting a mammal against neosporosis, comprising an immunologically effective amount of live cells of an attenuated strain of a species of Neosyora and a veterinarily acceptable carrier, wherein the strain is NCTS-8 which is present in MARC145 monkey kidney cells having ATCC accession accession No. CRL12230.

3. The vaccine of claim 2, further comprising an adjuvant.

4. The vaccine of claim 3, wherein the adjuvant is an oil-in-water emulsion.

5. A combination vaccine, comprising an immunologically effective amount of live cells of a an attenuated strain of a species of Neospora and a veterinarily acceptable carrier, wherein the strain is NCTS-8 which is present in MARC145 monkey kidney cells having ATCC accession No. CRL12230.

6. A composition comprising a veterinarily acceptable carrier and an immunologically effective amount of live cells of an attenuated strain of a species of Neosyora, wherein the strain is NCTS-8 which is present in MARC145 monkey kidney cells having ATCC accession No. CRL12230.

7. The composition of claim 6, further comprising an adjuvant.

8. The composition of claim 7, wherein the adjuvant is an oil-in-water emulsion.

First Hit Fwd Refs

L2: Entry 16 of 21 File: USPT Jun 6, 2000

US-PAT-NO: 6071737
DOCUMENT-IDENTIFIER: US 6071737 A

TITLE: Equine Neospora isolate and its uses

DATE-ISSUED: June 6, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Marsh; Antoinette E.	Columbia	MO		
Conrad; Patricia A.	Davis	CA		
Barr; Bradd C.	Davis	CA		

US-CL-CURRENT: 435/258.1

CLAIMS:

What is claimed is:

1. A biologically pure culture of equine Neospora having all the characteristics of ATCC Acession No. 209622 (NE1).

2. The culture of claim 1, which is of ATCC Accession No. 209622.

First Hit

End of Result Set

L2: Entry 21 of 21 File: JPAB Jun 23, 1998

PUB-NO: JP410167983A
DOCUMENT-IDENTIFIER: JP 10167983 A
TITLE: ATTENUATED LIVE NEOSPORA VACCINE

PUBN-DATE: June 23, 1998

INVENTOR-INFORMATION:

NAME	COUNTRY
DAVID, A BRAKE	
BYRON, L BLAGBURN	
DAVID, S LINDSAY	

ASSIGNEE-INFORMATION:

NAME	COUNTRY
PFIZER INC	
UNIV AUBURN	

APPL-NO: JP09310686
APPL-DATE: November 12, 1997

INT-CL (IPC): A61 K 39/00; A61 K 35/68; A61 K 39/002; A61 K 39/39; C12 N 1/00

ABSTRACT:

PROBLEM TO BE SOLVED: To obtain a live vaccine for neosporosis prepared from arm attenuated strain of a pathogenic protozoan of Neospora sp. and an attenuated strain useful for preventing clinical diseases and abortion in mammals.

SOLUTION: This live vaccine for neosporosis is a cultured product of a temperature-sensitive cell of a strain, derived from a pathogenic parent strain of Neospora sp. capable of manifesting the attenuated pathogenicity as compared with that of a parent strain of Neospora caninum, etc., and triggering an immureological reaction for protecting mammals against neosporosis when administered as the live vaccine.

COPYRIGHT: (C)1998,JPO

L3: Entry 12 of 35 File: USPT Apr 6, 2004

US-PAT-NO: 6716423
DOCUMENT-IDENTIFIER: US 6716423 B1

TITLE: Recombinant neospora antigens and their uses

DATE-ISSUED: April 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Conrad; Patricia A.	Davis	CA		
Barr; Bradd C.	Davis	CA		
Anderson; Mark L.	Davis	CA		
Sverlow; Karen W.	Vacaville	CA		

US-CL-CURRENT: 424/93.1; 424/184.1, 424/234.1, 424/93.7

CLAIMS:

What is claimed is:

1. A method for obtaining a normal calf from a bovine animal, comprising the steps of: (i) administering to the bovine animal a pharmaceutical composition comprising a pharmaceutically acceptable carrier and an immunogenically effective amount of a bovine Neospora tachyzoite; (ii) breeding the bovine animal; and (iii) obtaining a normal calf from the bovine animal.

2. The method of claim 1, wherein the bovine animal is a cow or heifer.

3. The method of claim 1, wherein the pharmaceutical composition is administered parenterally.

4. The method of claim 1, wherein the isolated bovine Neospora tachyzoite is attenuated.

5. The method of claim 1, wherein the bovine Neospora tachyzoite is selected from the group consisting of ATCC Accession No. 75710 (BPA1) and ATCC Accession Accession No. 75711 (BPA6).

6. A method for protecting a bovine animal from Neospora abortion, the method comprising the administration of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and an immunogenically effective amount of a bovine Neospora antigen, whereby the bovine animal is protected from abortion abortion induced by Neospora infection, wherein the bovine Neospora antigen is an isolated bovine Neospora tachyzoite of ATCC Accession No. 75710 (BPA1) or ATCC Accession No. 75711 (BPA6).

7. The method of claim 6, wherein the bovine animal is a cow or heifer.

8. The method of claim 6, wherein the pharmaceutical composition is administered to the bovine animal prior to breeding.

9. The method of claim 6, wherein the isolated bovine Neospora tachyzoite is attenuated.

10. The method of claim 6, wherein the pharmaceutical composition is administered parenterally.

11. A method for protecting a bovine animal from Neospora abortion, the method comprising the administration of a pharmaceutical composition comprising a pharmaceutically acceptable carrier and an immunogenically effective amount of an isolated bovine Neospora tachyzoite that is attenuated, whereby the bovine animal is protected from abortion induced by Neospora infection.

12. The method of claim 11, wherein the bovine animal is a cow or heifer.

13. The method of claim 11, wherein the pharmaceutical composition is administered to the bovine animal prior to breeding.

14. The method of claim 11, wherein the pharmaceutical composition is administered parenterally.

15. The method of claim 11, wherein the bovine Neospora tachyzoite is selected from the group consisting of ATCC Accession No. 75710 (BPA1) and ATCC Accession Accession No. 75711 (BPA6).

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L3: Entry 14 of 35 File: USPT Dec 2, 2003

US-PAT-NO: 6656479
DOCUMENT-IDENTIFIER: US 6656479 B2

TITLE: Attenuated live neospora vaccine

DATE-ISSUED: December 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Brake; David A	East Lyme	CT		
Blagburn; Byron L	Auburn	AL		
Lindsay; David S	Christiansburg	VA		

US-CL-CURRENT: 424/269.1; 424/258.1, 424/271.1, 424/273.1, 424/93.1, 424/93.2, 435/258.1, 435/69.1

CLAIMS:

We claim:

1. A live culture of cells of an attenuated strain of a species of Neosyora, wherein the strain is NCTS-8 which is present in MARC145 monkey kidney cells having ATCC accession No. CRL12230.

2. A vaccine for protecting a mammal against neosporosis, comprising an immunologically effective amount of live cells of an attenuated strain of a species of Neosyora and a veterinarily acceptable carrier, wherein the strain is NCTS-8 which is present in MARC145 monkey kidney cells having ATCC accession No. CRL12230.

3. The vaccine of claim 2, further comprising an adjuvant.

4. The vaccine of claim 3, wherein the adjuvant is an oil-in-water emulsion.

5. A combination vaccine, comprising an immunologically effective amount of live cells of a an attenuated strain of a species of Neospora and a veterinarily acceptable carrier, wherein the strain is NCTS-8 which is present in MARC145 monkey kidney cells having ATCC accession No. CRL12230.

6. A composition comprising a veterinarily acceptable carrier and an immunologically effective amount of live cells of an attenuated strain of a species of Neosyora, wherein the strain is NCTS-8 which is present in MARC145 monkey kidney cells having ATCC accession No. CRL12230.

7. The composition of claim 6, further comprising an adjuvant.

8. The composition of claim 7, wherein the adjuvant is an oil-in-water emulsion.

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What is claimed is:

1. An isolated polynucleotide molecule comprising a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:2.

2. An isolated polynucleotide molecule comprising a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID NO:1 from nt 205 to nt 777, the nucleotide sequence of SEQ ID NO:3 from nt 605 to nt 1304, and the nucleotide sequence of the GRA1-encoding ORF of plasmid pRC77 (ATCC209685).

3. An isolated polynucleotide molecule comprising a nucleotide sequence that hybridizes under conditions of 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS), 1mM EDTA at 65° C., and washing in 0.2 xSSC/0.1% SDS at 42° C., to the compliment of a polynucleotide molecule having a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO:2, wherein the isolated polynucleotide molecule can detect the presence of a Neospora-specific polynucleotide in a fluid or tissue sample from a Neospora-infected animal; provided that the isolated polynucleotide molecule does not encode a polypeptide having more than 90% amino acid sequence identity to a native GRA polypeptide from *Toxoplasma gondii*.

4. The polynucleotide molecule of claim 3, comprising a nucleotide sequence that hybridizes under conditions of 0.5 M $NaHPO_4$, 7% SDS, 1 mM EDTA at 65° C., and washing in 0.1xSSC/0.1% SDS at 68° C., to the complement of a polynucleotide molecule having a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO:2.

5. The polynucleotide molecule of claim 3, comprising a nucleotide sequence that hybridizes under conditions of 0.5 M $NaHPO_4$, 7% SDS, 1 mM EDTA at 65° C., and washing in 0.1xSSC/0.1% SDS at 68° C. to the complement of a polynucleotide molecule consisting of a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID NO:1 from nt 205 to nt 777, and the nucleotide sequence of SEQ ID NO:3 from nt 605 to nt 1304.

6. The isolated polynucleotide molecule of claim 3, which does not encode a polypeptide having more 80% amino acid sequence identity to a native GRA polypeptide from *Toxoplasma gondii*.

7. An isolated polynucleotide molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:1 from nt 1 to nt 204; SEQ ID NO:1 from nt 778 to nt 1265; SEQ ID NO:3 from nt 1 to nt 604; SEQ ID NO:3 from nt 605 to nt 855; SEQ ID NO:3 from nt 856 to nt 982; SEQ ID NO:3 from nt 983 to nt 1304; and SEQ ID NO:3 from nt 1305 to nt 1774.

8. A recombinant vector comprising a polynucleotide molecule comprising a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:2.

9. The recombinant vector of claim 8, wherein the nucleotide sequence of the polynucleotide molecule is selected from the group consisting of the nucleotide sequence of SEQ ID NO:1 from nt 205 to nt 777, the nucleotide sequence of SEQ ID NO:3 from nt 605 to nt 1304, and the nucleotide sequence of the GRA1-encoding ORF of plasmid pRC77 (ATCC 209685).

10. The recombinant vector of claim 9 which is plasmid pRC77 (ATCC 209685).

11. A recombinant vector comprising a polynucleotide molecule comprising a nucleotide sequence that hybridizes under conditions of 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS), lmM EBTA at 65° C., and washing in 0.2 xSSC/0.1% SDS at 42° C., to the compliment of a polynucleotide molecule having a nucleotide sequence that encodes the amino acid sequence of SEQ ID NO:2, wherein the polynucleotide molecule can detect the presence of a Neospora-specific polynucleotide in a fluid or tissue sample from a Neospora-infected animal; provided that the polynucleotide molecule does not encode a polypeptide having more than 90% amino acid sequence identity to a native GRA polypeptide from *Toxoplasma gondii*.

12. A host cell into which a polynucleotide molecule comprising a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:2, or a recombinant vector comprising said polynucleotide molecule, has been introduced.

13. A host cell into which a polynucleotide molecule, or a recombinant vector comprising said polynucleotide molecule, has been introduced, said polynucleotide molecule comprising a nucleotide sequence that hybridizes under conditions of 0.5 M $NaHPO_4$, 7% SDS, 1 mM EDTA at 65° C., and washing in 0.1 xSSC/0.1 % SDS at 68° C. to the complement of a polynucleotide molecule consisting of a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID NO:1 from nt 205 to nt 777, and the nucleotide sequence of SEQ ID NO:3 from nt 605 to nt 1 304, wherein the isolated polynucleotide molecule can detect the presence of a Neospora-specific polynucleotide in a fluid or tissue sample from a Neospora-infected animal, provided that the polynucleotide molecule does not encode a polypeptide having more than 90% amino acid sequence identity to a native GRA polypeptide from *Toxoplasma gondii*.

14. A method of preparing a polypeptide comprising the amino acid sequence of SEQ ID NO:2, comprising culturing a host cell into which a polynucleotide molecule comprising a nucleotide sequence encoding a protein comprising the amino acid sequence of SEQ ID NO:2, or a recombinant vector comprising said polynucleotide molecule, has been introduced, which polynucleotide molecule is in operative association with one or more regulatory elements, under conditions conducive to the expression of the polypeptide, and recovering the expressed polypeptide from the cell culture.

* * * * *

US006600027B1

(12) **United States Patent**
Krishnan et al.

(10) **Patent No.: US 6,600,027 B1**
(45) **Date of Patent: Jul. 29, 2003**

(54) **POLYNUCLEOTIDE MOLECULES ENCODING NEOSPORA PROTEINS**

(75) Inventors: **B. Rajendra Krishnan**, East Lyme, CT (US); **Rebecca Madura**, Westerly, RI (US); **Christine Yoder**, Salem, CT (US); **Becky Durtschi**, Ledyard, CT (US); **David A. Brake**, East Lyme, CT (US)

(73) Assignees: **Pfizer, Inc.**, New York, NY (US); **Pfizer Products, Inc.**, Groton, CT (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/276,438**

(22) Filed: **Mar. 25, 1999**

Related U.S. Application Data

(60) Provisional application No. 60/112,282, filed on Dec. 15, 1998, and provisional application No. 60/079,389, filed on Mar. 26, 1998.

(51) **Int. Cl.**[7] **C07H 21/02**; C07H 21/04; C12P 21/06; C12N 1/20; C12N 15/00

(52) **U.S. Cl.** **536/23.1**; 536/23.4; 536/23.5; 536/24.32; 435/320.1; 435/252.3; 435/69.1

(58) **Field of Search** 536/23.1, 23.4, 536/23.5, 24.32; 435/320.1, 252.3, 69.1

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(List continued on next page.)

Primary Examiner—Nita Minnifield
(74) *Attorney, Agent, or Firm*—Scully, Scott, Murphy & Presser

(57) **ABSTRACT**

The present invention provides isolated polynucleotide molecules comprising nucleotide sequences encoding GRA1, GRA2, SAG1, MIC1 and MAG1 proteins from *Neospora caninum*, as well as recombinant vectors, transformed host cells, and recombinantly-expressed proteins. The present invention further provides a polynucleotide molecule comprising the nucleotide sequence of the bidirectional GRA1IMAGI promoter of *N. caninum*. The present invention further provides genetic constructs based on the polynucleotide molecules of the present invention that are useful in preparing modified strains of Neospora cells for use in vaccines against neosporosis.

14 Claims, No Drawings

First Hit

L2: Entry 4 of 21 File: PGPB Oct 2, 2003

DOCUMENT-IDENTIFIER: US 20030185852 A1
TITLE: Parasitic protozoan isolate

Summary of Invention Paragraph:
[0012] The literature on live vaccines against N. caninum is limited. Atkinson et al. (1999) showed that infection of naive mice by the Nc-SweB1 isolate of N. caninum partially protected them against a severe infection by Nc-Liverpool. Lindsay et al. (1999) generated temperature sensitive mutants of N. caninum and demonstrated that they could prevent clinical signs associated with neosporosis in mice.

Detail Description Paragraph:
[0119] Lindsay D S, Lenz S D, Blagburn B L & Brake D A (1999) Characterization of temperature-sensitive strains of Neospora caninum in mice Journal of Parasitology 85, 64-67.

Previous Doc Next Doc Go to Doc#
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L3: Entry 16 of 35 File: USPT Sep 10, 2002

DOCUMENT-IDENTIFIER: US 6448252 B1
TITLE: Treatment of equine protozoal myeloencephalitis

Other Reference Publication (46):
David S. Lindsay et al., "Demonstration of Synergistic Effects of Sulfonamides and Dihydrofolate Reductase/Thymidylate Synthase Inhibitors Against Neospora caninum Tachyzoites in Cultured Cells, and Characterization of Mutants Resistant to Pyrimethamine," AJVR, vol. 57, Jan. 1996, pp.. 68-72.

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10507781 PMID: 10608449

Phenotypic characterisation of a Neospora **caninum** temperature - sensitive **strain in normal and immunodeficient mice.**

Dreier K J; Stewarter L W; Kerlin R L; Ritter D M; Brake D A

Animal Health Biological Discovery and Drug Safety Evaluation (RLK), Pfizer Central Research, Pfizer Inc., Groton, CT 06340, USA.

International journal for parasitology (ENGLAND) Oct 1999, 29 (10) p1627-34, ISSN 0020-7519 Journal Code: 0314024

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The in vivo persistence, immunogenicity and pathogenicity of a recently described **temperature - sensitive** (ts) strain from **Neospora** caninum, NCts-8, was investigated in normal and immunodeficient mice. Groups of BALB/c and SCID/Bg mice were infected s.c. with 5 x 10(6) wild-type NC-1, control NCts-8 (pass 0) or NCts-8 tachyzoites prepared at four in vitro passage levels (pass 7, 13, 21 and 28). For persistence and immunogenicity studies, BALB/c mice were bled and sacrificed at 4, 6 or 8 weeks p.i. Sera were analysed by IFAT and brain tissues examined for lesions by histology and tested for parasite presence by PCR. For pathogenicity studies, SCID/Bg mice were monitored by clinical signs and survival time. Results from parasite persistence experiments demonstrated microscopic lesions and PCR positive brain tissues in NC-1 infected mice. In contrast, brain tissues from NCts8-infected groups were consistently negative by histology and PCR. Based on IFAT titres, all parasite strains were immunogenic, although parasite-specific IgG levels were lower in the NCts-8 infected groups. Results from pathogenicity studies in SCID/Bg mice demonstrated a significantly ($P < 0.0001$) longer mean survival time in NCts-8 vs NC-1 infected groups. In addition, there was no significant difference in mean survival time between control NCts-8 and experimental passage NCts-8 infected mice. Collectively, these studies demonstrate that the NCts-8 strain maintains a stable phenotype following multiple passages in vitro, and possesses an attenuated, shorter persistence phenotype in vivo compared with the parental wild-type NC-1.

Descriptors: Coccidiosis--parasitology--PS; * **Neospora** --physiology--PH; Animals; Antibodies, Protozoan--blood--BL; Brain--pathology--PA; DNA, Protozoan--analysis--AN; Mice; Mice, Inbred BALB C; Mice, SCID; **Neospora** --genetics--GE; **Neospora** --immunology--IM; **Neospora** --pathogenicity--PY ; Phenotype; Polymerase Chain Reaction; Temperature; Virulence

CAS Registry No.: 0 (Antibodies, Protozoan); 0 (DNA, Protozoan)

Record Date Created: 20000120

Record Date Completed: 20000120

?logoff hold

13092196 PMID: 8720241

Demonstration of synergistic effects of sulfonamides and dihydrofolate reductase/thymidylate synthase inhibitors against Neospora **caninum tachyzoites in cultured cells, and characterization of mutants resistant to pyrimethamine.**

Lindsay D S ; Butler J M; Rippey N S; Blagburn B L
Department of Pathobiology, Auburn University, AL 36849-5519, USA.

American journal of veterinary research (UNITED STATES) Jan **1996** , 57 (1) p68-72, ISSN 0002-9645 Journal Code: 0375011
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
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OBJECTIVE: To examine the efficacies of combinations of 7 sulfonamides and 5 dihydrofolate reductase/thymidylate synthase (DHFR/TS) inhibitors against tachyzoites of **Neospora** caninum in cultured cells. Mutant tachyzoites that were resistant to pyrimethamine were produced and examined for resistance to other DHFR/TS inhibitors. DESIGN AND PROCEDURES: After 5 days of treatment, a cell culture flask lesion-based assay was used to determine efficacies of combinations of sulfonamides and DHFR/TS inhibitors against N caninum tachyzoites and to evaluate the sensitivity of pyrimethamine-resistant mutants of N caninum to test agents. Cultured cells that were infected with the appropriate strains of N caninum and treated or not treated (controls) with test agents were examined. Mutations were induced by chemical mutagenesis with N-methyl-N'-nitro-N-nitrosoguanidine or by selection for growth in permissive concentration of pyrimethamine. RESULTS: Synergism was detected for combinations of pyrimethamine, ormetoprim, trimethoprim, or diaveridine with the sulfonamides. Methotrexate did not have improved efficacy when combined with sulfonamides. Two mutants were produced that were resistant to pyrimethamine. Both mutants were resistant to other DHFR/TS inhibitors. Both mutants remained resistant to pyrimethamine in the absence of continuous exposure to the agent, indicating that the induced resistance was stable. Synergism was detected for combinations of DHFR/TS inhibitors and sulfonamides against these pyrimethamine-resistant mutants. CONCLUSIONS: Combinations of suboptimal concentrations of sulfonamides with suboptimal concentrations of DHFR/TS inhibitors results in improved efficacy of the agents in a cell culture assay. Stable resistance to pyrimethamine can be induced in N caninum tachyzoites by use of chemical mutagenesis or by selection. CLINICAL RELEVANCE: In vitro evidence indicated that combination treatment, using sulfonamides and DHFR/TS inhibitors, may be effective in treating **neosporosis** .